Original Article

Prediction of Gestational Diabetes by Measuring First Trimester Maternal Serum Uric Acid Concentration

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common complication in pregnancy, affecting more than 10% pregnancies worldwide. However, the true underlying causes remain to be fully elucidated. **Aim:** This study aimed at searching for any relation between first trimester uric acid concentration and the development of GDM. **Subjects and Methods:** The study was conducted on 250 first trimester pregnant females at risk of diabetes mellitus attending the outpatient clinic of Tanta University Hospital. All cases underwent estimation of first trimester-fasting blood sugar and maternal serum uric acid concentration. Between 24 and 28 weeks' gestation random blood sugar and glucose challenge test were done. Positive cases were confirmed by 3 h glucose tolerance curve. **Results:** The results demonstrated an association between first trimester maternal serum uric acid concentration obesity and GDM. Approximately, 41.4% (60/145) of non-diabetic women were at first quartile, while 44.8% (47/105) of the diabetic women were at fourth quartile. **Conclusion:** We concluded that the cut-off level of maternal serum uric acid of 4 mg/dl in the first trimester was associated with developing GDM. Therefore, we suggest that serum uric acid level should be done as routine test during the first antenatal care visit.

KEY WORDS: Impaired fasting glucose, multiple logistic-regression analysis, type 2 diabetes mellitus, uric acid

INTRODUCTION

It is well recognized that gestational diabetes mellitus (GDM), defined as two or more elevated glucose values obtained during a 3-h oral glucose tolerance test (OGTT), is associated with increased perinatal complications adverse pregnancy outcomes are also more frequent with milder degrees of carbohydrate intolerance.[1]

GDM and preeclampsia (PE) are two common complications in pregnancy, affecting more than 10% pregnancies worldwide. However, the true underlying causes of these two conditions remain to be fully elucidated. Although both conditions were diagnosed first during pregnancy, it is uncertain whether they originate prior to or during pregnancy.[2]

Several studies have now shown that, compared to their peers, women who go on to develop GDM later in pregnancy have biochemical abnormalities that can be detected in the first trimester including increased levels of uric acid.[3,4] To date, there has been limited study of pre-gravid function of women who go on to develop GDM. These limited data, however, do support the concept of metabolic dysfunction prior to pregnancy in this patient population.[5-7]

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidase. Hypoxia and ischemia of the placenta and cytokines such as, interferon induce the expression of xanthine oxidase and therefore, increase the production of uric acid and also reactive oxygen species.[8]

Many studies have indicated that serum uric acid is associated with hypertension, obesity, hyper insulinemia and dyslipidemia, suggesting that it could be part of the cluster of factors of the metabolic syndrome.[9]

In uncomplicated pregnancies, serum uric acid concentrations fall in early pregnancy 25-35% due to an elevation in renal clearance secondary to increased glomerular filtration rate or reduced proximal tubular

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reabsorption and due to changes in its production rate.[10-12] Later in pregnancy the serum uric acid levels increase, possibly due to raised fetal production, decreased binding to albumin and a decline in uric acid clearance until toward the end of pregnancy when they approach non-pregnant values.[13-16]

The aim of this study is to determine the accuracy and clinical value of first trimester maternal serum uric acid concentration in predicting the subsequent development of gestational diabetes.

SUBJECTS AND METHODS

We conducted this study on 250 first trimester pregnant females susceptible of diabetes mellitus attending the antenatal clinic of Tanta University Hospital. The study was approved by the institutional review board and informed written consent was obtained from all subjects.

This study was organized on 250 first trimester pregnant females susceptible to diabetes mellitus attending the antenatal clinic of Tanta University Hospital.

Selection criteria

Maternal age greater than 35 years, severe obesity, patient with past history of gestational diabetes, positive family history of type 2 diabetes, history of delivery of large-for-gestational-age infant, presence of glycosuria, history of multiple gestation, history of unexplained poor obstetric outcome, polyhydramnios as proved by US.

Women were excluded from the study if they had multiple fetuses, chronic hypertension, renal disease, diabetes, other pre-existing medical conditions or history of illicit drug use.

Methods

All females in the study were subjected to complete history taking and clinical and ultrasound examination.

Estimation of maternal serum uric acid concentrations[17] and fasting blood sugar concentration during the first trimester

Estimation of random blood sugar during second trimester (≥200 mg/dl patient is diabetic). Glucose challenge test (GTT) was done as a confirmatory test.[18]

Statistical analysis of data was conducted, using SPSS Version 16.0 (Chicago Illinios, USA.) program. Receiver operating characteristic (ROC) curves was done to evaluate the performance of classification schemes in which there is one variable with two categories by which subjects are classified. One of the three points that divide a range of data or population into four equal parts; the first quartile (also called the lower quartile) is the number below which lies the 25% of the bottom data; the second quartile (the median) divides the range in the middle and has 50% of the data below it; the third quartile (also called the upper quartile) has 75% of the data below it and the top 25% of the data above it.[19]

RESULTS

As regards gravidity, it has been found that 23.2% (58/250) of the studied patients were third gravida, 21.2% (53/250) were fifth gravida, 19.6% (49/250) were second gravida, 18.0% (45/250) were primigravida, and similar percentage were fourth gravida.

Regarding parity, it clear that 25.2% (63/250) of the studied cases were nullipara, 24.8% (62/250) were para one, 18.8% (47/250) were para two, 18.4% (46/250) were para three, and 12.8% (32/250) were para four.

Concerning past history, 72.0% (180/250) of the studied cases had negative history of gestational diabetes, while 28.0% (70/250) had positive history of gestational diabetes.

About family history of type 2 diabetes, 70.4% (176/250) of the studied cases had negative history of type 2 diabetes, while 29.6% (74/250) had positive family history of type 2 diabetes.

Vis-à-vis obesity, 38.4% (96/250) of our cases were obese, 28.0% (70/250) were overweight, 20.8% (52/250) were morbid obese, and 12.8% (32/250) were of normal weight.

Apropos diabetes, 58.0% (145/250) of the studied cases were non-diabetic, while of the 42.0% (105/250) of the cases were diabetic. Table 1 shows the baseline descriptive statistics of the mean (SD) of age, body mass index, blood sugar and uric acid. The relationship between the uric acid category in relation to diabetes, and obesity in relation to diabetes are shown in Tables 2 and 3 respectively. Figures 1 and 2 show the Receiver operating characteristic between serum uric acid and body mass index, and the correlation between serum uric acid and body mass index respectively.

Table 1: Descriptive statistics of different parameters

	Min	Max	Mean	SD
Age in years	22.00	32.00	27.268	3.136
Body mass index (Kg/m^2)	21.48	49.31	31.365	5.132
FBS-1st trimester (Mg/dl)	65.00	108.00	79.580	8.485
Serum uric acid (Mg/dl)	1.80	8.50	3.667	0.907
Glucose tolerance test (Mg/dl)				
Fasting BS	71.00	182.00	117.409	23.451
BS after 1 h	123.00	260.00	182.322	25.270
BS after 2 h	111.00	235.00	166.278	22.611
BS after 3 h	97.00	210.00	151.878	22.814

FBS – Fasting blood sugar; BS – Blood sugar

Table 2: Uric acid category in relation to diabetes

Uric acid category	Non-diabetic	Diabetic	Total
1st quartile (1.8-3.1 mg/dl)			
N	60	2	62
%	41.4	1.9	24.8
2nd quartile (3.1-3.5 mg/dl)			
N	46	17	63
%	31.7	16.2	25.2
3rd quartile (3.5-4 mg/dl)			
N	24	39	63
%	16.6	37.1	25.2
4th quartile (4-8.5 mg/dl)			
N	15	47	62
%	10.3	44.8	24.8
Total			
N	145	105	250
%	100.0	100.0	100.0
χ^2	83.431		
P value	0.0001		

Uric acid category in relation to diabetic, it demonstrated that, uric acid 1st quartile (1.8-3.1 mg/dl) were found in 41.4% non-diabetic case and 1.9% were diabetic respectively, 2nd quartile (3.1-3.5 mg/dl) were found in 31.7% non-diabetic case and 16.2% were diabetic, in 3rd quartile (3.5-4 mg/dl) were found in 16.6% non-diabetic case and 37.1%, were diabetic while 4th quartile (4-8.5 mg/dl) were found in 10.3% non-diabetic case and 44.8% were diabetic. Most of the non-diabetic women (41.4%) were at 1st quartile, while most of the diabetic women (44.8%) were at 4th quartile. There were highly statistical significant differences between uric acid category and diabetic women (*P*=0.0001)

Table 3: Obesity in relation to diabetes

Obesity	Non-diabetic	Diabetic	Total
Normal weight			
N	12	20	32
%	8.3	19.0	12.8
Over weight			
N	49	21	70
%	33.8	20.0	28.0
Obese			
N	55	41	96
%	37.9	39.0	38.4
Morbid obese			
N	29	23	52
%	20.0	21.9	20.8
Total			
N	145	105	250
%	100.0	100.0	100.0
χ^2			9.784
P value			0.020

The relationship between obesity and diabetes in the studied cases. Notice the significant increase in the prevalence of obesity among diabetic women

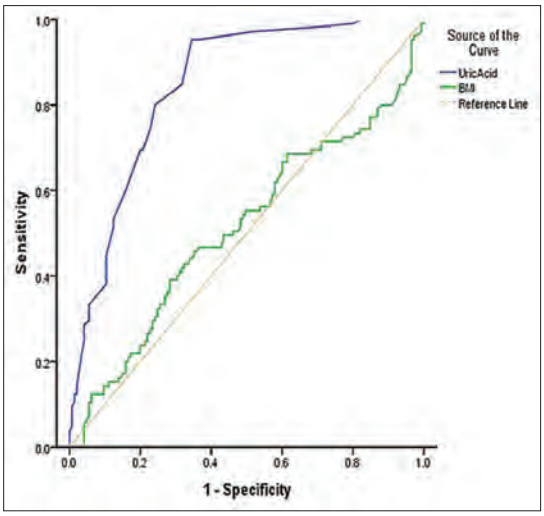

Figure 1: Receiver operating characteristic curve shows that, there is no significant relation between serum uric acid and body mass index (Area under the curve 0.844)

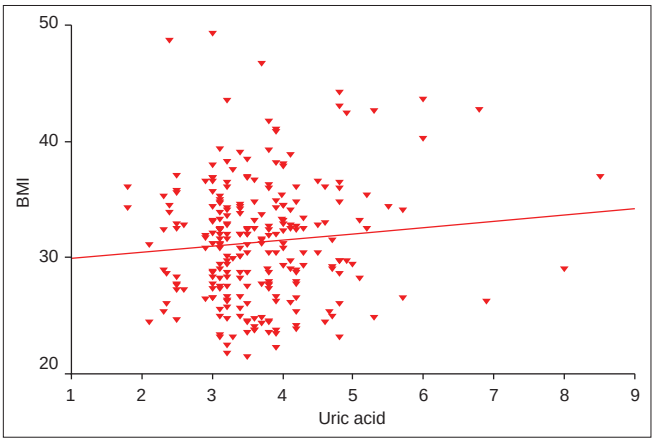

Figure 2: This curve shows that, there is no correlation between serum uric acid and body mass index (r=0.093, *P*=0.143)

DISCUSSION

The term abnormal glucose tolerance (AGT) related to pregnancy has been used to describe the population of women with an elevated GTT. This condition is fairly common with an incidence of 17-27% depending on diagnostic criteria and population. Identified risk-factors for AGT include marked obesity, diabetes in first-degree relatives, older maternal age, and current glycosuria, previous delivery of a macrocosmic infant and non-white ethnicity.[1]

During pregnancy, serum uric acid is higher at 24-28 week's gestation in women diagnosed with GDM compared to women without diabetes.[20]

Because high-level of uric acid is associated with insulin resistance and predates development of type 2 diabetes in non-pregnant adults, we assumed that higher uric acid blood concentrations during the first trimester would be linked with the elaboration of GDM.

The current research confirmed our postulation as it demonstrated the presence of a striking association between first-trimester uric acid concentrations and the risk of developing GDM, where 44.8% of patients with elevated uric acid concentrations >4 mg/dl developed GDM.

In agreement with our results, Katherine, showed that first-trimester hyperuricemia was associated with an increased risk of developing GDM, independent of body mass index. Katherine found that uric acid ≥3.6 mg/dl early in pregnancy is associated with a 3-fold increased risk of developing GDM.[11]

Yoo and associates reported the association of uric acid with insulin resistance in the non-pregnant population and

concluded that hyperuricemia is a risk-factor for developing type 2 diabetes mellitus.[21]

A number of studies suggest that metabolic traits (e.g., glucose, uric acid, and lipids) beyond personal diabetes risk-factors are important to adequately establish future risk of type 2 diabetes. Most attempts to substantially improve diabetes prediction with measurements from genetics and transcriptomics have not been successful, and whether serial measurements might decrease variations in non-genetic biomarkers, resulting in a more precise estimation of their concentrations, is not known.[22-24]

Hyperuricemia is also closely associated with insulin resistance, as it is potentially an independent predictor of cardiovascular disease.[21,25-27] The present authors and others have recently demonstrated that increased serum uric acid is an independent risk-factor for non-alcoholic fatty liver disease, which is closely related to insulin resistance.[28,29]

A meta-analyses by Kodama *et al.*[30] revealed that elevated serum uric acid is positively associated with the development of type 2 diabetes mellitus. Indeed, both cross-sectional and cohort investigations have provided evidence that increased serum uric acid is an independent risk-factor for diabetes mellitus.[31-35] However, some of these investigations were limited to male subjects only,[31,32] while others demonstrated that there might be gender-dependent differences in its significance.[27,33-37]

The current investigation portrayed that the cut-off level of maternal serum uric acid of 4 mg/dl in the first trimester was associated with developing GDM. Therefore, we suggest that serum uric acid level should be done as routine test during the first antenatal care visit.

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